PND43

## COST-EFFECTIVENESS ANALYSIS OF PEGINTERFERON BETA-1A IN THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS IN SCOTLAND

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**OBJECTIVES:** Self-injectable disease-modifying therapies (DMTs) are the first-line standard of care for relapsing-remitting multiple sclerosis (RRMS) in Scotland: Interferon beta (IFNβ)-1a (22mcg and 44mcg three times/week, and 30mcg once/week), IFNβ-1b 250mcg every other day, and glatiramer acetate (GA) 20mg once/day. Peginterferon beta-1a (PEG-IFN; 125mcg subcutaneous every two weeks) is a new DMT with less frequent dosing which may improve treatment adherence. The pivotal ADVANCE trial showed benefits of PEG-IFN versus placebo on relapses and disability progression, but its long-term clinical and economic consequences versus other DMTs are still unknown. This analysis assessed the cost-effectiveness of PEG-IFN versus self-injectable DMTs from the National Health System perspective in Scotland. **METHODS:** A Markov cohort economic model, published and accepted by health technology assessment authorities, was adapted for this analysis. The model predicts disability progression (measured by the Expanded Disability Status Scale [EDSS]) and occurrence of relapses and other adverse events (AEs), and translates them into quality-adjusted life-years and costs. The natural history data were obtained from the placebo arm of the ADVANCE trial extrapolated with data from the London, Ontario database for EDSS transition probabilities and from a large population-based MS survey for relapse rates. A network meta-analysis was conducted to estimate the comparative efficacy of each treatment versus placebo. Costs (in 2014 British Pounds) of drug acquisition, disease management, relapses, and AEs were from public databases and literature. Clinical and economic outcomes were projected over 30 years and discounted at 3.5% per year. **RESULTS:** Over 30 years, PEG-IFN yielded greater clinical benefits and cost savings compared with IFNβ-1a 22mcg IFNβ-1a 30mcg, and IFNβ-1b 250mcg. Compared with GA 20mg and IFNβ-1a 44mcg, the incremental cost-effectiveness ratios were £17,821 and £4,121, respectively. Deterministic and probabilistic sensitivity analyses confirmed that the results were robust. **CONCLUSIONS:** PEG-IFN is a cost-effective treatment for patients with RRMS in Scotland.

PND44

## COST-EFFECTIVENESS OF FIRST-LINE DISEASE-MODIFYING THERAPIES (DMTS) FOR RELAPSING-REMITTING MS (RRMS)

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**OBJECTIVES:** Teriflunomide 14 mg is the only first-line DMT with significant reduction in both relapses and 12-week disability progression in 2 pivotal clinical trials. Cost-effectiveness of teriflunomide 14 mg once daily orally vs other first-line DMTs for RRMS (oral dimethyl fumarate [DMF] 240 mg twice daily; subcutaneous glatiramer acetate (GA) 20 mg daily, interferon ([IFN] β-1a 44 µg 3×/week, and IFNβ-1b 250 µg every other day; intramuscular IFNβ-1a 30 µg once weekly) and best supportive care (BSC) were evaluated in the Finnish healthcare payer setting. **METHODS:** The primary outcome was incremental cost-effectiveness ratio (ICER; €/quality-adjusted life-year [QALY] gained vs nondominated alternatives). Markov cohort modeling with a 20-year time horizon (3%/year discount rate) was employed. During each 1-year modeling cycle, patients could maintain their Expanded Disability Status Scale (EDSS) score or experience progression, develop secondary-progressive MS (SPMS), have EDSS progression in SPMS, or experience relapse with/without hospitalization or death. Patient characteristics, standardized mortality ratios, and an RRMS progression matrix were derived from a Finnish MS registry. Specific annual adverse event (AE) risks were included. A mixed-treatment comparison informed treatment effects. EQ-5D quality-of-life estimates and Finnish direct costs were associated with EDSS scores, relapses, and AEs. Robustness of base case results was tested with probabilistic sensitivity analyses (PSAs). **RESULTS:** Teriflunomide was less costly with higher QALYs vs GA and IFNs. DMF brought marginally more QALYs than teriflunomide (0.129 over 20 years); this difference was associated with higher costs. The ICER for DMF vs teriflunomide was 78,092, and teriflunomide had the lowest ICER of 17,326 vs BSC. In the PSAs, teriflunomide had over 50% cost-effectiveness probabilities, with willingness-to-pay values below €94,000/QALY gained vs other first-line DMTs. **CONCLUSIONS:** The cost-effectiveness of teriflunomide 14 mg once daily vs DMF twice daily and dominance over other first-line DMTs for RRMS were demonstrated in this Finnish study.

PND45

## COST-EFFECTIVENESS ANALYSIS OF PEGINTERFERON BETA-1A IN THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS IN IRELAND

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**OBJECTIVES:** Peginterferon beta-1a (PEG-IFN; 125mcg subcutaneous every 2 weeks) is a new disease-modifying therapy (DMT) for relapsing-remitting multiple sclerosis (RRMS) that may improve treatment adherence by reducing the frequency of administration. The pivotal ADVANCE trial showed benefits of PEG-IFN versus placebo on relapses and disability progression, but its long-term clinical and economic consequences versus other DMTs are still unknown. This analysis assessed the cost-effectiveness of PEG-IFN versus other self-injectable DMTs (Interferon beta-1a 22mcg and 44mcg three times/week, and 30mcg once/week; interferon beta-1b 250mcg every other day; and glatiramer acetate 20mg once/day) from the Health Services Executive perspective in Ireland. **METHODS:** An economic model, using a Markov cohort approach, published and accepted by health technology assessment authorities, was adapted for this analysis. The model predicts disability progression (measured by the Expanded Disability Status Scale [EDSS]) and occurrence of relapses and other adverse events (AEs), and translates them into quality-adjusted life-years (QALYs) and costs. Natural history data were obtained from the placebo arm of the ADVANCE trial extrapolated with data from the London, Ontario database for EDSS transition probabilities and from a large population-based MS survey for relapse rates. A network meta-analysis was conducted to estimate the comparative efficacy of each treatment versus placebo. Costs (in 2013 Euro) of drug acquisition, disease management, relapses, and AEs were from public databases and literature. Clinical and economic outcomes were projected over 30 years and discounted at 3.5% per year. **RESULTS:** Over 30 years, treatment with PEG-IFN resulted in higher QALYs and cost-savings compared with all commercially available self-injectable DMTs in Ireland. Deterministic sensitivity analyses confirmed the results were robust. Probabilistic sensitivity analyses indicated that the incremental cost-effectiveness ratio was below the willingness-to-pay threshold (€45,000 per QALY) in >85% of 5,000 replications versus all comparators. **CONCLUSIONS:** PEG-IFN is a cost-effective treatment for patients with RRMS in Ireland.

PND46

## COST-EFFECTIVENESS ANALYSIS OF GLYBERA FOR THE TREATMENT OF LIPOPROTEIN LIPASE DEFICIENCY

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**OBJECTIVES:** Glybera is the first gene therapy drug for lipoprotein lipase deficiency (LPLD), which was approved by European Commission in 2012. Before the approval of Glybera, no effective treatment was available for LPLD. Patients with LPLD have to restrictively control fat intaken and are still more likely to suffer recurrent acute pancreatitis and eruptive xanthomas. Although Glybera can effectively improve the health conditoin of patients with LPLD, it is still controversial to price the gene therapy at 1.1 million euros. This study assesses the relative costs and effectiveness of Glybera compared to no treatment for LPLD from a societal perspective. **METHODS:** We developed a Markov model that tracked a cohort of patients through the three disease states of LPLD progression, defined by the symptoms of pancreatitis. We evaluated the effectiveness of the noval gene therapy based on published clinical trial data. We derived quality of life utility scores and costs data for each disease state from the published literature. We estimated the discounted costs, quality-adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICERs). Univariate sensitivity analyses were conducted to assess the impact of parameter uncertainty on our results. **RESULTS:** The incremental cost-effective ratio (ICER) of Glybera was € 51,789/QALY gained when compared with no intervention. Correspondingly, the net monetary benefit (NMB) is € 667,478, given the willingness-to-pay (WTP) is € 114,875. One-way sensitivity analyses were performed to investigate the model robustness. The analyses illustrated that the model was robust to the majority transition probabilities and utility of each health state. **CONCLUSIONS:** Although the price is high, Glybera is a cost-effective treatment for lipoprotein lipase deficiency compared with no treatment based on available clinical data. This conclusion is robust to sensitivity analyses.

PND47

## COST-EFFECTIVENESS ANALYSIS OF GINKGO BILOBA EXTRACT (EGB761® - TANAKAN®) FOR THE TREATMENT OF DEMENTIA IN THE CZECH REPUBLIC

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**OBJECTIVES:** To assess the cost-effectiveness of EGb761® for the treatment of mild dementia due to Alzheimer's disease (AD) and vascular dementia (VaD) in the Czech Republic in comparison to no treatment or acetylcholinesterase inhibitor (AChEI-donepezil; only AD). **METHODS:** Developed ten-year Markov cohort model with half-year cycle length projects outcomes (Quality-Adjusted Life-Years-QALYs; Life-Years Gained-LYGs) and costs of treatment for patients with AD and VaD aged 65 years from payers' perspective. Model health states are defined by the severity of dementia according to Mini-Mental State Examination (MMSE), i.e. no&minimal/mild/moderate/moderately severe/severe dementia and by death. Treatment schemes of dementia, which reflect current management, differ depending on severity of disease and assessed interventions. Transition probabilities and utilities were taken from published literature. Drug costs (EGb761®€63/half-year, donepezil €94/half-year) and costs of mild/moderately severe/severe dementia (€192/€318/€1,709 per half-year) were derived based on statement of KOLs and reimbursed lists. Costs and outcomes were discounted by 3%. Probability sensitivity analysis (PSA; 3,000 iteration) was performed with willingness-to-pay (WTP) threshold of 3 times GDP per capita in the Czech Republic (i.e. €44,000). **RESULTS:** EGb761® was dominant compared to no treatment in both mild AD and mild VaD while generating cost savings of €560 and €355 and gaining 0.2150QALYs/0.1287LYGs and 0.1841QALYs/0.11439LYGs over a 10-year horizon. In comparison to active therapy in mild AD, EGb761® is slightly less efficient (loss of 0.0025QALYs/0.0001LYGs), but also cheaper (by €35) than AChEI in a 10-year horizon. PSA showed that probability of EGb761®to be cost-effective varies from 50% to 84% at the WTP threshold. **CONCLUSIONS:** EGb761® represents a cost-saving intervention with more QALY gained, i.e. dominant therapy compared to no pharmacotherapy in treatment of mild dementia in 10 years. EGb761® shows very similar results (slightly cheaper and less efficient) in comparison to AchEI (e.g. donepezil) in the therapy of mild AD.

PND48

## SYSTEMATIC REVIEW OF ECONOMIC EVALUATIONS OF TREATMENTS IN EPILEPSY

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**OBJECTIVES:** The objective of this literature review was to explore the existing evidences regarding cost-effectiveness of interventions used to treat epilepsy. **METHODS:** A systematic literature review was performed using the PICO method: Population was patients suffering from epilepsy; Intervention and Comparators were any treatments, including non-pharmacological treatments, and Outcomes were ICERs. The literature search was performed with the NHS EED filters using MEDLINE, EMBASE and PubMed from January 2005 to May 5th, 2015. **RESULTS:**